

### **Remarks**

The Applicants have amended Claims 20 and 30 to place them into better condition for allowance. Claim 20 now includes the subject matter of Claims 21 and 22 as well as the description set forth on page 13 at paragraph 2. Claim 30 has also been amended to include the subject matter of Claim 31. Claims 21, 22 and 31 have accordingly been cancelled.

Turning now to the merits, this invention relates a method and a device for processing at least one substance in a reservoir of a microdosing device which is a micropipette or a microdispenser. Conventionally, micropipettes or microdispensers have been used for uptaking or delivering small liquid quantities (microdroplets). It should be noted that the term “microdispenser” is a technical term as used in the relevant art. Reference is made, e.g., to Papen (see the Abstract, line 2). The same is true for the term “micropipette”.

An object of this invention is to improve the function and broaden the application range of the above-mentioned microdosing devices. A solution is a solid carrier material arranged in the reservoir of the microdosing device. A substance to be collected or brought into reaction with another reaction partner is collected in the reservoir by repeatedly uptaking a solution or suspension of this substance and binding the substance and delivering (releasing) the liquid without the substance from the reservoir. After each step of uptaking the solution or suspension, binding and releasing, an increased portion of the substance to be collected is connected with the solid carrier material. After several repetitions, an enrichment of the substance is obtained in the reservoir. After this enrichment (collection), one of two alternative steps follows.

First, an elution agent can be introduced into the reservoir for separating the bound substance

from the carrier material. Under the influence of the elution agent, the collected substance is released from the solid carrier into the liquid within the reservoir. Accordingly, the concentration of the substance in the reservoir is essentially increased.

Second, a reaction partner can be introduced into the reservoir for starting a reaction with the collected substance.

An essential feature of the invention is the arrangement of the solid carrier in the reservoir of the microdosing device. During the whole procedure, the carrier material does not leave the reservoir. This provides a completely new function for the microdosing device.

Within a biochemical process, a substance can be concentrated or subjected to a reaction with the microdispenser or micropipette followed by dispensing the collected or modified substance to a substrate. The microdosing device can be used as a reaction container without losing the dispenser function.

The Applicants acknowledge the rejection of Claims 20 – 28 and 30 – 36 as being anticipated by Tajima. The Applicants respectfully submit that Claim 20 is novel over Tajima. Tajima does not disclose collecting (concentration) of substance in the reservoir of a microdosing device as claimed, followed by uptaking an elution agent or a reaction partner. In sharp contrast, Tajima discloses (see in particular Fig. 13, steps 15 – 19) to arrange magnetic particles (being the carrier material) in the reservoir of a “chip” (step 15), introducing certain reagents into the reservoir (steps 16, 17 and 18) and discharging the product of the reaction into an external reservoir (step 19).

Claim 20 is novel over Papen. Papen does not disclose collection of a substance in the reservoir according to the second step of the claimed method.

The subject of Claim 30 is novel over Tajima. Tajima does not disclose a microdosing device being a micropipette or a microdispenser containing a solid carrier material with a binding-active surface. On the other hand, the subject of Claim 30 is novel over Papen since Papen does not disclose the provision of a drive device outside the reservoir of a microdosing device. Withdrawal of the rejection of Claims 20 – 28 and 30 – 36, based on Tajima, is accordingly respectfully requested.

The Applicants acknowledge the rejection of Claims 29 and 37 – 38 over the hypothetical combination of Papen with Tajima. The Applicants respectfully submit that those claims are patentable over the hypothetical combination for the following reasons. First, the claimed collecting step (second step) is neither taught nor suggested in Tajima. As mentioned above, the claimed method defines not only a reaction of the substance bound to the carrier, but first a collection of the substance in the reservoir followed by elution or reaction. Papen is silent with regard to any processing step to be provided within the reservoir of the microdispenser. Thus, hypothetically combining Tajima and Papen cannot yield the claimed method.

The subject matter of Claim 30 is not obvious over a combination of Tajima and Papen. First, it is not obvious to provide magnetic particles within the reservoir of a microdosing device. A skilled person immediately would recognize that the function of the microdosing device essentially is influenced by the formation of pressure pulses within the reservoir. The skilled person would avoid materials within the reservoir to avoid distortion of the pressure pulses for activating the microdosing device. Therefore, the skilled person would not combine Tajima and Papen.

Even if a hypothetical combination of both references was made, the combination would still

not teach or suggest the subject matter of Claim 30. The device of the invention contains a drive device for holding and repeatedly moving the carrier material. The drive device of the invention is able to move the carrier material within the reservoir according to a plurality of movement sequences. The drive device (e.g., a magnet) of Tajima is not able to move the carrier material in the reservoir. If the magnet is separated from the chip, the carrier material is released from the reservoir but not moved within the microdosing device. The Applicants accordingly respectfully request withdrawal of the rejection of Claims 29 and 37 – 38 based on the hypothetical combination.

In light of the foregoing, the Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



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